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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,672	05/09/2006	Annelies Resink	BJS-3665-178	9794

23117 7590 02/27/2009

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
ARCHIE, NINA	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
02/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,672	RESINK ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/9/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 1-14-09. Claims 1-23 are pending. Claims 21-23 are withdrawn from consideration as being drawn to non-elected inventions. Claims 13-20 are currently under examination..

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

3. The specification is objected for containing an obvious typographical error. Specifically, encephalopathy is misspelled (see pg. 2 lines 10-15). Appropriate correction is advised. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

4. The information disclosure statement filed on 5/9/2006 has been considered. An initialed copy is enclosed.

Election/Restrictions

5. Applicant's election of Group I (claims 13-20) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Objections

6. Claims 17-19 are objected to because of the following informalities: As to claims 13-19, the claim contains the acronym BSE. While acronyms are permissible shorthand in the claims, the first recitation should include the full recitation followed by the acronym in parenthesis. As to claim 13, encephalopathy is misspelled. Appropriate correction is required.

As to claims 13, 17, and 18 are objected to as being drawn to non-elected inventions. Groups I, detailed above, read on patentably distinct sequences. Each sequence is patentably distinct because they are structurally different and a further restriction has been applied to Group I with the election of SEQ ID NO: 1. Applicant is reminding that examination will be restricted to only the elected nucleotide sequence and should not be construed as a species election.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

7. Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 13-20 are drawn to a method of detecting the presence or the risk of developing an encephalopathy in a mammal generally (claim 13-16) and BSE specifically (claims 17-19); comprising determining the presence in a biological sample from the mammal, of a target molecule selected consisting of: a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases, b) a nucleic acid having a sequence complementary to a sequence according to a), c) a functional analogue of a nucleic acid according to a) or b) originating from another species or a natural variant, or d) a polypeptide coded by a nucleic acid according to a) to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal.

The specification states "through extensive research based on a innovative approach, different additional BSE markers have been identified and validated by hybridization experiments, enabling the development of a presymptomatic test that can be used on blood from a live mammal". The specification states that the identified marker was given in sequences such as SEQ ID NO: 1 (see pg. 2 lines 10-15). Additionally clones were hybridized with probes produced from biological material from naturally or experimentally infected cows and healthy cows used as controls. As a result 15 clones were found to show a deregulation between healthy versus infected condition. Thus SEQ ID NO: 1 is purportedly able to detect deregulation between healthy versus infected condition. However no marker, including SEQ ID NO: 1 has been demonstrated to detect the presence or the risk of developing an encephalopathy in a mammal. SEQ ID NO: 1 is a genetic marker that is derived from Bovine Spongiform Encephalopathy. Even though the specification specifically discloses SEQ ID NO: 1 as being a genetic marker the gene has not been identified. The specification does not disclose any other information on the gene SEQ ID NO: 1 regarding its claimed function (detecting an encephalopathy or the risk of developing one). Furthermore, the specification does not disclose the expression level or if any expression level exists of SEQ ID NO: 1 (or any fragment, complement etc.) in a healthy individual. As a result Applicant has not shown the correlation of SEQ ID NO: 1 (or any fragment, complement etc.) with the function as directed with the aforementioned above, given that the gene is not identified and there is no correlation that can be made with regard to the presence of an encephalopathy much less the risk of developing an encephalopathy.

Moreover, the scope of the claims includes numerous structural variants/analogues, and the genus is highly variant because a significant number of structural differences between genus members are permitted. Furthermore the scope of the claim includes a nucleic acid having a sequence complementary to SEQ ID NO: 1 and a polypeptide coded by SEQ ID NO: 1 being an indication of the presence or the risk of developing an encephalopathy in said mammal. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, using target molecules to detect the presence or the risk of developing an encephalopathy in said mammal alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a

representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

As to the aforementioned method, the claims are drawn to a large number functional analogue of variants and a polypeptide coded by variants having different possibilities of changes to the amino acid sequence of SEQ ID NO: 1. The specification does not teach an example of any functional analogue of variants and a polypeptide coded by variants that comprise the method of detecting the presence or the risk of developing an encephalopathy in a mammal.

Without disclosure of the a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases; b) a nucleic acid having a sequence complementary to a sequence according to a); c) a functional analogue of SEQ ID NO: 1 or b) originating from another species or a natural variant; or d) a polypeptide coded by SEQ ID NO: 1 to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal for any method; the written description is not deemed to be fulfilled and the specification lacks proper written description of the claimed method as set forth *supra*. This issue is best resolved by Applicants pointing to the specification by page and line number where description of the claimed invention is set forth. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases; b) a nucleic acid having a sequence complementary to a sequence according to a); c) a functional analogue of SEQ ID NO: 1 or b) originating from another species or a natural variant; or d) a polypeptide coded by SEQ ID NO: 1 to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antigens. Therefore, in accordance with the Guidelines, the description is not deemed representative and thus does not meet the written description requirement.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register,

Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Enablement

8. Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for any method of detecting the presence or the risk of developing an encephalopathy in a mammal, comprising determining the presence in a biological sample from the mammal, of a target molecule selected consisting of: a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases, b) a nucleic acid having a sequence complementary to a sequence according to a), c) a functional analogue of a nucleic acid according to a) or b) originating from another species or a natural variant, or d) a polypeptide coded by a nucleic acid according to a) to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).
There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;
(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention

The claims are drawn to a method of detecting the presence or the risk of developing an encephalopathy in a mammal generally and BSE specifically, comprising determining the presence in a biological sample from the mammal, of a target molecule selected consisting of: a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases, b) a nucleic acid having a sequence complementary to a sequence according to a), c) a functional analogue of a nucleic acid according to a) or b) originating from another species or a natural variant, or d) a polypeptide coded by a nucleic acid according to a) to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal.

The breadth of the claims

The product being used to detect the presence or the risk of developing an encephalopathy in a mammal comprises:

a) a nucleic acid comprising a sequence of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases;

b) a nucleic acid having a sequence complementary to a sequence according to a);

c) a functional analogue of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases; or a nucleic acid having a sequence complementary sequence to a sequence according to SEQ ID NO:1 originating from another species or a natural variant; or

d) a polypeptide coded by SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases; or a nucleic acid having a sequence complementary sequence to a sequence according to SEQ ID NO:1 originating from another species or a natural variant; or a functional analogue of SEQ ID NO: 1 or a fragment thereof containing at least 5, preferably 6, 7, 8, 9, or 10 consecutive bases; or a nucleic acid having a sequence complementary sequence to a sequence according to SEQ ID NO:1 originating from another species or a natural variant is overly broad. Therefore it is hard for one skilled in the art

to determine if steps c) and d) can be used for detecting the presence or the risk of developing an encephalopathy in a mammal.

The Quantity of Experimentation Required

The quantity of experimentation required to practice the invention as claimed would be undue as it would require novel and unknown species that will correlate to steps a) b) c) and d) as set forth *supra* to detect the presence detecting the presence or the risk of developing an encephalopathy in a mammal. Since the specification fails to provide particular guidance for detecting the presence of or the risk of developing an encephalopathy as set forth supra it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Guidance in the specification

The specification states "through extensive research based on a innovative approach, different additional BSE markers have been identified and validated by hybridization experiments, enabling the development of a presymptomatic test that can be used on blood from a live mammal". The specification states that the identified marker was given in sequences such as SEQ ID NO: 1 (see pg. 2 lines 10-15). Additionally clones were hybridized with probes produced from biological material from naturally or experimentally infected cows and healthy cows used as controls. As a result 15 clones were found to show a deregulation between healthy versus infected condition. Thus SEQ ID NO: 1 is purportedly able to detect deregulation between healthy versus infected condition. However no marker, including SEQ ID NO: 1 has been demonstrated to detect the presence or the risk of developing an encephalopathy in a mammal. SEQ ID NO: 1 is a genetic marker that is derived from Bovine Spongiform Encephalopathy. Even though the specification specifically discloses SEQ ID NO: 1 as being a genetic marker the gene has not been identified. The specification does not disclose any other information on the gene SEQ ID NO: 1 regarding its claimed function (detecting an encephalopathy or the risk of developing one). Furthermore, the specification does not disclose the expression level or if any expression level exists of SEQ ID NO: 1 (or any fragment, complement etc.) in a healthy individual. As a result Applicant has not shown the correlation of

SEQ ID NO: 1 (or any fragment, complement etc.) with the function as directed with the aforementioned above, given that the gene is not identified and there is no correlation that can be made with regard to the presence of an encephalopathy much less the risk of developing an encephalopathy.

Moreover, the scope of the claims includes numerous structural variants/analogues, and the genus is highly variant because a significant number of structural differences between genus members are permitted. Furthermore the scope of the claim includes a nucleic acid having a sequence complementary to SEQ ID NO: 1 and a polypeptide coded by SEQ ID NO: 1 being an indication of the presence or the risk of developing an encephalopathy in said mammal. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, using target molecules to detect the presence or the risk of developing an encephalopathy in said mammal alone is insufficient to describe the genus. As to the aforementioned method, the claims are drawn to a large number functional analogue of variants and a polypeptide coded by variants having different possibilities of changes to the amino acid sequence of SEQ ID NO: 1. The specification does not teach an example of any functional analogue of variants and a polypeptide coded by variants that comprise the method of detecting the presence or the risk of developing an encephalopathy in a mammal.

Therefore, the specification as filed fails to provide particular guidance demonstrating a reasonable extrapolation with method of detecting the presence as set forth supra.

Working examples

The specification does not provide any working examples of any of the claimed target molecules being able to perform the function set forth in the preamble of the claim.

In conclusion, the claimed inventions are not enabled for a method of detecting the presence as set forth supra comprising c) a functional analogue of a nucleic acid according to a) or b) originating from another species or a natural variant, or d) a polypeptide coded by a nucleic acid according to a) to c), the presence of said target molecule in the sample being an indication of the presence or the risk of developing an encephalopathy in said mammal. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention. The product being used to detecting the presence or the risk of developing an encephalopathy in a mammal comprising: step c) and step d) as set forth supra is overly broad. Furthermore, Applicant has not disclosed a complementary sequence of SEQ ID NO: 1 in step b) which will encode a different protein to detect the presence or the risk of developing an encephalopathy in a mammal. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 13 recites the phrase “natural variant”. However, neither the claim nor the specification clearly defines nor sets forth the meaning or means to assess "target". Prior art states that "target" is defined in the art as selective, specific, or nonspecific with respect to cells. Therefore, the skilled artisan would not be readily apprised of the metes and bounds of "natural variant" nor how to assess such. It is unclear how to interpret what is considered "target" and inasmuch as it is not a recognized term and not defined in the specification.

Status of the Claims

10. No claims are allowed.

Claims 13-20 are rejected.

Claims 21-23 are withdrawn from consideration.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina Archie
Examiner
Art Unit 1645

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645